Clinical Case Report

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Treatment with verapamil for restoration of sinus rhythm in atrial fibrillation with rapid ventricular response

A case report

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Abstract

Rationale: Atrial fibrillation (AF) is a common arrhythmia disease that can cause thromboembolic disease and/or heart failure, resulting in increased mortality. Propafenone, amiodarone, and flecainide are recommended for converting AF to sinus rhythm. Beta blockers, verapamil, diltiazem, and digoxin are recommended for controlling AF with fast ventricular rate (VR). In this case report, we found that verapamil successfully converted AF into sinus rhythm.

Patient concerns: A 92-year-old woman presented with fast VR AF with a history of coronary heart disease, hypertension, and diabetes.

Diagnoses: Verapamil can successfully convert AF into sinus rhythm.

Interventions and Outcomes: The patient was treated with amiodarone or propafenone, yet still had AF. After stopping amiodarone and propafenone, the patient was given verapamil to control the VR, and following 9 days of treatment the patient switched to sinus rhythm. When verapamil treatment was stopped, the patient experienced AF recurrence. Upon receiving verapamil again, the AF again converted into sinus rhythm.

Lessons: For the treatment of AF, nondihydropyridine calcium antagonists can be tried in the absence of antiarrhythmic drugs.

Abbreviations: AER = atrial electrical remodeling, AF = atrial fibrillation, ASR = atrial structural remodeling, VR = ventricular rate.

Keywords: atrial electrical remodeling, atrial fibrillation, conversion, verapamil

1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical disease. As the world's population ages, it is predicted that AF will affect 6 to 12 million people in the United States by 2050 and 17.9 million people in Europe by 2060.[1] Numerous studies have confirmed that age is an independent risk factor for AF. The Framingham study showed an AF incidence of 0.5% in people 50 to 59 years old, 1.8% in 60 to 69 years old, 4.8% in 70 to 79 years old, and 8.8% in 80 to 89 years old. AF incidence significantly increases in people older than 60, with incidence doubling every 10 years.[2] According to a study published by the European Heart Rhythm Association, the prevalence of AF is about 1% in people younger than 60 years old, 12% in people 75 to 84 years old, and >1/3 after 80 years old.[3] AF brings high economic burdens to peoples' lives, and increased AF prevalence increases the risk of death as its complications seriously threaten human survival and health. In cardiovascular disease, AF is an independent risk factor for heart failure and stroke. Antiarrhythmic drugs do not have ideal effects on AF, and radiofrequency ablation has limitations. This article describes a senile patient with AF who successfully converted to sinus rhythm by trying a variety of antiarrhythmic drugs.

2. Case presentation

The patient, female, 92 years old, had a history of coronary heart disease, hypertension, and diabetes and was treated with oral medicine year-round. Two days before admission, the patient developed palpitations, chest tightness, and other discomforts. The patient could not sleep on her back as it would cause intermittent coughing and an increased pulse rate of 90 beats/min via self-test. The physical examination upon admission showed body temperature 36.2°C, pulse 132 beats/min, blood pressure 120/80 mm Hg, breathing 20 times/min. Breathing sounded clear in the lungs via auscultation, with small rales becoming audible at the lung bases. Heart rate was measured at 155 beats/min with completely uneven rhythm: the intensity of the first heart sound

Editor: N/A.

XW and YL contributed to the investigation. Data curation was done by XW and LC. XW and DL contributed to the resources. The original draft was prepared by XW and JL. The final draft was reviewed and edited by XW, JL, GQ, and WT.

The authors have no funding or conflicts of interest to disclose.

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Medicine (2019) 98:23(e15892)

Received: 2 January 2019 / Received in final form: 15 April 2019 / Accepted: 29 April 2019

http://dx.doi.org/10.1097/MD.0000000000015892

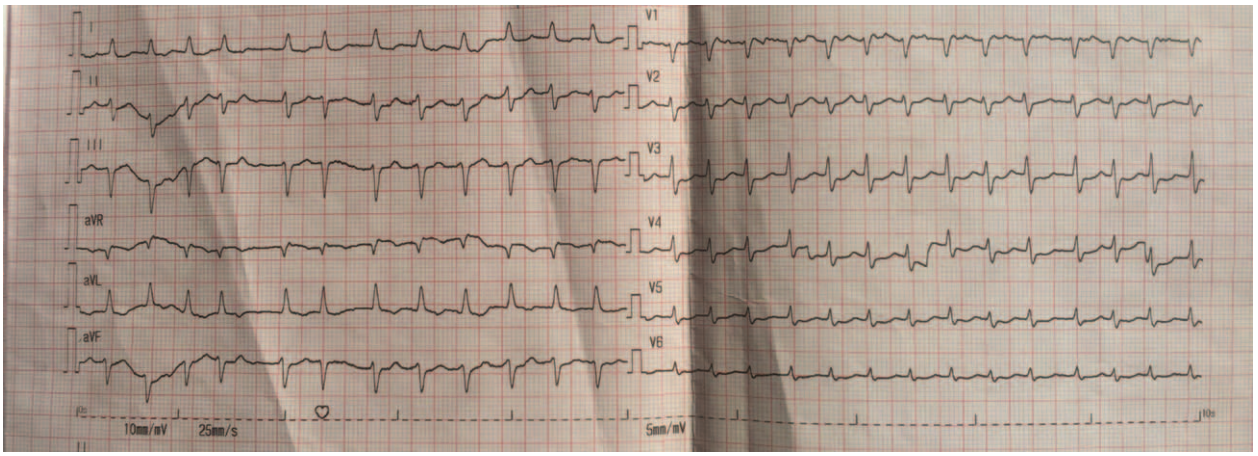

Figure 1. Electrocardiogram of the patient at admission.

was unequal and the first auscultation area of the aortic valve had 3/6-grade systolic jet-like noises with conduction to the neck. The bilateral dorsal artery showed diminished pulsation, and there was slight edema in the left lower limb. Electrocardiogram (2017–9–12): AF, ventricular rate (VR) 155 beats/min, the ST segment of I aVL V3–6 leads ST segment depression was depressed by 0.05 to 0.1 mv (Fig. 1). Cardiac color Doppler ultrasound showed aortic valve degeneration with stenosis (aortic valve anterior blood flow velocity 3 ms^{-1}), mild hypertrophy of the left ventricular myocardium, a slightly enlarged left atrium (39 mm), reduced left ventricular diastolic function, and normal left ventricular systolic function under the resting state.

For patients with valvular heart disease, surgery is generally not considered due to their advanced age. For the initial AF, metoprolol tartrate tablets were used to control VR and amiodarone was used for conversion. We used the CHA_2DS_2-VAS scoring system to assess the patient's thromboembolic risk[4,5] and found a score of 4 points. A bleeding risk assessment was performed using the HAS-BLED scoring system with a score of 2 points.[6] The patient was given rivaroxaban to prevent thromboembolism. When the cumulative dose of amiodarone was 10.55 g, the patient still had AF rhythm with VR fluctuating between 100 and 120 beats/min, but QTc was significantly prolonged at 0.509 s, so the patient stopped taking amiodarone. After intravenous application of propafenone, the patient's blood pressure decreased significantly, so propafenone was stopped. Then, based on the application of metoprolol tartrate tablets, diltiazem was administered. The patient's heart rate did not improve under the control and her blood pressure significantly decreased. We replaced diltiazem with 40 mg verapamil 3 times a day, and the patient converted to sinus rhythm with a heart rate of 70 beats/min after 9 days of application. We then stopped administering verapamil and provided amiodarone to prevent AF recurrence. Six days later, the patient again presented with AF. At that point, the patient stopped taking amiodarone and was again administered 40 mg verapamil 3 times a day. After 5 days, the patient switched to sinus rhythm and was discharged. At the time of discharge, the patient had sinus rhythm (Fig. 2) and no discomfort such as shortness of breath. Metoprolol tartrate was applied throughout the treatment process, with the dosage changed from 25 mg twice a day to 3 times a day. The detailed

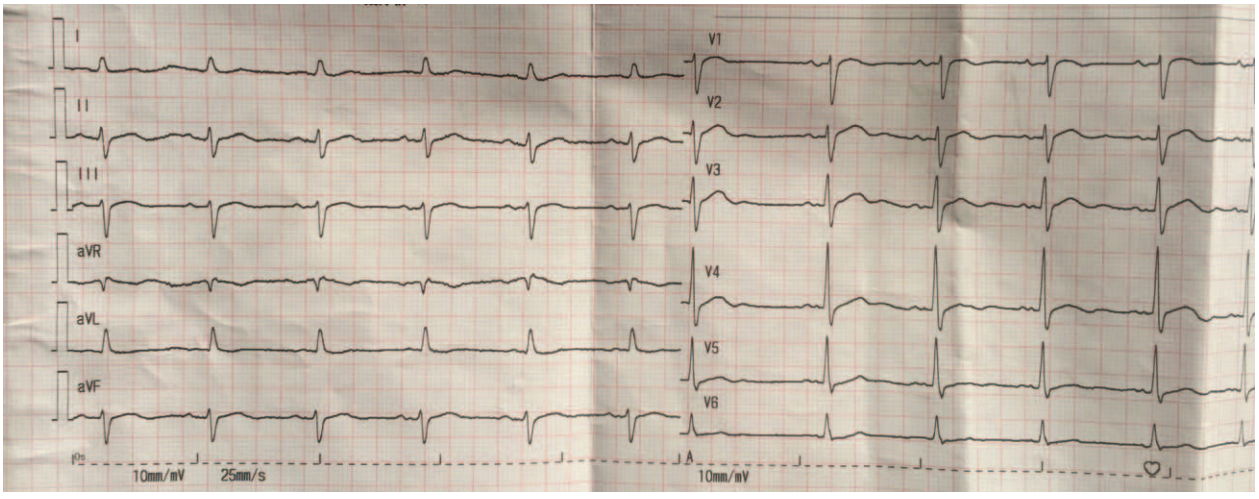

Figure 2. Electrocardiogram of the patient at discharge.

medication process undertaken while in hospital is shown in Table 1. The patient continued to take verapamil 40 mg 3 times a day, metoprolol tartrate 25 mg twice a day, and rivaroxaban 10 mg once a day once discharged from the hospital. The verapamil dosage was gradually reduced and was discontinued 2 months following discharge. The patient received follow-up electrocardiograms every month, and AF was not observed.

3. Discussion and conclusion

AF is the most common arrhythmia in elderly patients. AF incidence increase with increased age, and prevalence is higher in elderly patients or patients with other diseases such as hypertension, heart failure, coronary heart disease, valvular heart disease, obesity, diabetes, or chronic kidney disease. AF can increase patient mortality, especially due to sudden death, heart failure, or stroke. In the present case, the patient had a history of age-related degenerative heart valve disease, coronary heart disease, hypertension, and type 2 diabetes, and the incidence of AF is doubled. The patient was initially diagnosed with AF and a heart rate of 155 beats/min. The primary task was to reduce the VR and to start anticoagulation and transfer therapy.

According to the 2016 ESC/EACTS Atrial Fibrillation Management Guide, the recommended drugs for controlling VR are beta blockers, digoxin, and the calcium antagonists diltiazem or verapamil.[7] We first chose metoprolol tartrate to control the patient's VR and amiodarone to convert heart rhythm. To guide our choice regarding anticoagulant drugs, we used the CHA2DS2-VAS scoring system to evaluate the patient's embolization risk. The patient scored 4 points, indicating that anticoagulant therapy was recommended. The patient was considered to have no mechanical heart valve and no mitral moderate to severe stenosis. As the Guide prefers new anticoagulant drugs, we chose rivaroxaban for the patient. The causes of AF in this patient were advanced age, moderate aortic stenosis, hypertension, and diabetes. The mechanism of AF is more complicated: atrial structural remodeling (ASR) and atrial electrical remodeling (AER) play important roles in AF occurrence and maintenance.[8] Structural heart disease, high blood pressure, and other diseases can lead to changes in atrial structure, and AF itself can induce ASR slowly and progressively. The concept of AER was first proposed by Wijffels et al in 1995.[9] The electrical remodeling was mainly characterized by a shortening of the effective atrial refractory period, a decrease in the frequency adaptability of the atrial effective refractory period, an increase in the refractory period, and a decrease in the conduction velocity. These events are conducive to the occurrence and maintenance of AF. Many researchers have also confirmed that AER plays a key role in the occurrence and maintenance of AF.[10–12] Some believe that intracellular calcium overload is a prominent feature of AER.[13] Studies have shown that mitochondrial dysfunction and oxidative stress in atrial cells can lead to the occurrence and maintenance of AF.[14] Verapamil is a calcium channel blocker that can reduce damage from mitochondrial and oxidative stress by inhibiting the NF-kappa B signaling pathway until AF is terminated. Verapamil can also block AER by inhibiting the ERK/MAPK-signaling pathway.[15] A possible mechanism for how the use of verapamil drove the conversion of AF to sinus rhythm in this patient is through reducing calcium influx, reducing intracellular calcium overload, and inhibiting AER. Diltiazem and verapamil are both L-type calcium channel blockers, but the patient's blood pressure dropped when taking diltiazem. Studies have shown that diltiazem has a stronger antihypertensive effect than verapamil.[16] We theorize that diltiazem may also have converted the patient's AF to sinus rhythm if it did not cause the patient's blood pressure to drop. It is well known that verapamil is used to decrease heart rate, yet the role of verapamil in converting AF to sinus rhythm has not been reported. This case suggests that individualized comprehensive treatment should be advocated for these types of diseases. For elderly patients with multiple underlying diseases and liver- and kidney-function decline, drug utilization and metabolic rates change, so it is necessary to develop and adjust treatment plans quickly and comprehensively.

4. Consent for publication

Informed written consent was obtained from the patient for publication of this case report and the accompanying images

Acknowledgments

We are grateful to the patient, who gave her informed consent for publication. I would like to express my gratitude to all those who helped me during the writing of this case report.

Table 1

The detailed medication process undertaken while in hospital.

Drug and dosage	Course	Outcome		
		Heart rhythm	Heart rate (beats/min)	Blood pressure (mm Hg)
Amiodarone total amount 10.5 g	From 2017–9–12 to 2017–9–29	AF	100–120	110/60
Propafenone total amount 455 mg	2017–9–30	AF	110	85/50
Diltiazem 90 mg qd p.o.	From 2017–10–1 to 2017–10–10	AF	110–130	87/52
Verapamil 40 mg tid p.o.	From 2017–10–11 to 2017–10–19	Sinus rhythm	70	110/65
Amiodarone 0.2 g qd p.o.	From 2017–10–20 to 2017–10–25	AF	132	107/61
Verapamil 40 mg tid p.o.	From 2017–10–26 to 2017–10–30	Sinus rhythm	72	108/56

AF = atrial fibrillation, g = gram, mg = milligram, p.o. = per os (oral), qd = quaque die (once a day), tid = ter in die (3 times a day).

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Writing – original draft: Xiaoou Wang, Jie Lin.
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References

[1] Schnabel RB, Yin XY, Gona P, et al. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham heart study: a cohort study. Lancet 2015;386:154–62.
[2] Kannel WB, Abbott RD, Savage DD, et al. Epidemiologic features of chronic atrial fibrillation: the Framingham study. N Engl J Med 1982;306:1018–22.
[3] Camm AJ, Kirchhof P, Lip GY, et al. Guidelines for the management of atrial fibrillation The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J 2010;31:2369–429.
[4] Lip GY, Nieuwlaat R, Pisters R, et al. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 2010;137:263–72.
[5] January CT, Wann LS, Alpert JS, et al. American College of Cardiology/ American Heart Association Task Force on Practice Guideline2014AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol 2014;64:2305–7.
[6] Pisters R, Lane DA, Nieuwlaat R, et al. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. Chest 2010;138:1093–100.
[7] Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J 2016;37:2893–962.
[8] Allessie M, Ausma J, Schotten U. Electrical, contractile and structural remodeling during atrial fibrillation. Cardiovasc Res 2002;54:230–46.
[9] Wijffels MC, Kirchhof CJ, Dorland R, et al. Atrial fibrillation begets atrial fibrillation. A study in awake chronically instrumented goats. Circulation 1995;92:1954–68.
[10] Hobbs WJ, Fynn S, Todd DM, et al. Reversal of atrial electrical remodeling after cardioversion of persistent atrial fibrillation in humans. Circulation 2000;101:1145–51.
[11] Raitt MH, Kusumoto W, Giraud G, et al. Reversal of electrical remodeling after cardioversion of persistent atrial fibrillation. J Cardiovasc Electrophysiol 2004;15:507–12.
[12] Ohashi N, Mitamura H, Tanimoto K, et al. A comparison between calcium channel blocking drugs with different potencies for T- and L-type channels in preventing atrial electrical remodeling. J Cardiovasc Pharmacol 2004;44:386–92.
[13] Yue L, Feng J, Gaspo R, et al. Ionic remodeling underlying action potential changes in a canine model of atrial fibrillation. Circ Res 1997;81:512–25.
[14] Bukowska A, Schild L, Keilhoff G, et al. Mitochondrial dysfunction and redox signaling in atrial tachyarrhythmia. Exp Biol Med 2008;233:558–74.
[15] Cheng W, Zhu Y, Wang H. The MAPK pathway is involved in the regulation of rapid pacing-induced ionic channel remodeling in rat atrial myocytes. Mol Med Rep 2016;13:2677–82.
[16] Saseen JJ, Carter BL, Brown TE, et al. Comparison of nifedipine alone and with diltiazem or verapamil in hypertension. Hypertension 1996;28:109–14.